

The pupil opens slowly with two tiny adhesions stretching. Atropin 1%. Hot fomentations every three hours were ordered.

August 19. Patient had a comfortable night. The pupil is well dilated this morning. This condition dragged along till September before quieting down.

November 20, 1918. The patient returned. He has had no trouble since last seen until about a week ago when the left eye started to bother again. It was red and inflamed and the iris sluggish in reaction. 1% atropin instilled. The pupil dilated at once. 1% atropin three times a day. Hot fomentations were ordered.

November 21. The condition is not as good this morning. The patient was sent to Dr. Montgomery for a throat examination. Dr. Montgomery reports pus in both tonsils and advised their removal at once. They were removed the following morning and the patient was not seen again until December 6. The eye immediately began to quiet down after the tonsils were removed and is fairly white and quiet to-day. All local treatment was stopped.

December 12. Eye white and quiet to-day.

December 27. Has had no further trouble.

Recurrent Iritis.

Case VIII, 12845 (Dr. A. C. M.)—Miss A. B., 36.

First attack 1913. Second 1916, in April. Third November 1916. Another in May in 1917 lasting two or three months.

I first saw the patient on December 4, 1918, with a history of pain in the left eye for the past few days. The eye was congested and the iris discolored. 2% atropin was instilled. The pupil only dilated a little above. On questioning, the patient apparently has chronic tonsilitis. She was sent to Dr. Montgomery for an examination, who reported the tonsils were full of pus. We explained to the patient that this was probably the cause of the recurrent inflammation in her eye, and advised immediate removal as otherwise these attacks would continue. Hot fomentations and 1% atropin were ordered every four hours. The patient had the tonsils removed and the eye immediately began to quiet down and treatment was gradually discontinued.

The patient was seen again on December 30. Within a week the eye was white and quiet and has practically been so since the tonsils were removed.

The patient says this is the shortest and least painful attack she has ever had.

Recurrent Ulcers Cornea.

Case IX, 2510—Mr. F. J. L.

Was first seen in July, 1917. There was a history of gonorrheal infection two years previously with severe complications. The patient was in the hospital several months with perineal drainage for prostatic abscess. One year after this he had corneal ulcers which were very stubborn in healing. He was having some urethral disturbance at this time and under treatment. The left eye had been bothering for a couple of days. There was a small area of infiltration in the lower part of the cornea, which was soft and pulpy. It was touched with tincture of iodine and treated with a collyrium of zinc sulphate and boracic acid, and yellow oxide of mercury ointment for the next two weeks when it quieted down.

He was seen again on June 19, 1918, with a similar recurrence following an acute exacerbation of his urethral disturbance. I only saw the patient twice at this time as he left for Mexico.

He came in again on April 4, 1919, with a new infiltration in the cornea following a fresh urethral infection and reports having had several recurrences during the past year. The case is still under treatment but always clears up with the disappearance of the urethral infection.

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MULTIPLE PRIMARY TUMORS.*

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The great majority of malignant tumors occurring in the human body are of one type only, either sarcoma or carcinoma, and moreover, they appear to originate from one focus only, whether a single cell or a group of cells. This mode of origin was formerly considered practically the only way in which tumors originated. A single cell, or group of cells, took on a form of malignant degeneration, increased in number, became differentiated from the tissues surrounding them and eventually formed metastases. The original focus was considered to be the sole point of origin.

This view was later controverted by Peterson, who showed in the study of a case of mammary carcinoma, that the focus of origin could be multicentric. He made serial sections of the tumor, reconstructed them in wax, superimposed the various layers, one upon the other, and by cutting away the stroma, had a model of cellular elements of the tumor. He was thus able to show that these cell masses, spreading out in all directions had several independent points of origin. Indeed, Peterson takes the ground that such a pluricentric method of origin is the rule, rather than the exception.

Wooley¹ reports a case of adrenal new growth, where the new formation can be seen springing from several distinct areas in the cortex. It is not very frequent that we can prove such a multiplicity of points of origin. Usually the growth has advanced to such a degree that there is only one large mass. In the adenomatous and adeno-carcinomatous growths of the ovary (where practically always both organs are involved), at operation, one only may seem to be involved with no other secondary growth. However, if the other be allowed to remain in situ, it frequently must be removed at a secondary operation and then presents the same type of disturbance.

Case 1. The case which called my attention to the subject of multiple tumors, was that of a man who presented a melano-sarcoma of the mediastinum, with a primary carcinoma of the esophagus. The patient, age 56, was admitted to the hospital complaining of difficulty in swallowing, accompanied by substernal pain of increasing intensity, with the recent onset of difficulty in respiration. His trouble began nine months previous, when he had a painful sensation upon swallowing. This difficulty in swallowing progressively increased. Vomiting also began and was almost a daily occurrence. After the passage of bougies, he was able to swallow better for a time. Six months later his voice became hoarse and this condition gradually became worse. He complained of pain beneath the sternum and at a corresponding area in his back. This was worse when he sat down and he was most comfortable when standing or lying.

His general health had been good. In 1893, he had a ruptured urethra resulting from a fall and had a posterior incision to drain the bladder. For the past two or three years, he has had spells every five or six weeks, lasting about a day, when he was obliged to urinate every hour. There was no pain or burning sensation. Had tonsillitis as a child, but no difficulty in swallowing until the present time. There have been no digestive disturbances, except about sixteen years ago, when he had an "inflammation of the stomach" which

* Read before the Santa Clara County Medical Society.

required about four to five months' treatment. He had worked as a miner in Australia and South America for many years and had frequently given demonstrations of swallowing broken glass. His last demonstration had caused some pain in his throat and forced him to give up the practice. He gives a history of lues, has always been a heavy drinker and smoker. Average weight until onset of his trouble has been 175 pounds. He now weighs 128 pounds.

Examination shows a markedly emaciated old man. Pupils react well; eye grounds normal. **Neck:** marked venous and carotid pulsation on right side, less marked on the left. **Voice:** very hoarse; on lower lip a small nevus. **Glands:** in the left axilla there is a mass the size of a hen's egg, hard and not tender; not adherent to the skin. Right axillary enlarged, supraclavicular nodules right and left, many palpable inguinals. **Urine:** negative. **Blood:** reds 4,500,000; whites 8300; hemoglobin 80 per cent.; polys. 67 per cent.; lymphocytes 30 per cent.; large lym. 1 per cent.; eosinophiles 2 per cent.; transitionals 3 per cent. **Feces:** occult blood, marked reaction. **Wassermann:** negative. X-ray showed an irregular narrowing of the esophagus at the bifurcation of the trachea with considerable mediastinal thickening.

It was felt that the clinical history with the above laboratory findings justified the diagnosis of a carcinoma of the esophagus at the bifurcation of the trachea with metastases to the axillary and supraclavicular glands. However, the tumor mass in the axilla on removal and sectioning proved to be a melano-sarcoma, as shown by the following extracts from the pathologic report: "Tumor mass the size of a hen's egg, black in color, soft and fluctuating. Section shows a semi-solid central portion of black material resembling tar, with a more solid, yet friable periphery. The outermost layer is fibrous and shows blood vessels running in various directions. The tissue consists, for the most part, of pigment cells varying in size, arrangement and pigmentation. The cells are large, spindle-shaped, others round and polymorphous. Many contain numerous dark brown pigment granules. So numerous are these in some of the cells that the nuclei are hidden, while others contain no pigment granules. There are all gradations between these extremes. Several multi-nucleated cells are seen. The stroma consists of a small amount of connective tissue supporting blood-vessels. The blood-vessels are being invaded by tumor cells. Several small areas of lymphoid tissue are seen scattered throughout the section. There is a fairly dense fibrous tissue capsule which is invaded by pigment cells."

As cases of primary melano-sarcoma originating in the lining epithelium of the esophagus had been reported, the diagnosis was changed to that of primary melano-sarcoma of the esophagus with axillary metastases.

Autopsy however proved it to be different. In the apices of both lungs were found extensive adhesions and evidences of old consolidations. The liver was enlarged, but no nodulations or tumor formations were present. There were chains of enlarged glands in both supra-clavicular triangles, more marked on the right side. These glands varied in size up to 1 cm. in length and were mostly of a deep black color. Both axillae contained numerous chains of glands accompanying the vessels, those of the left axilla being much larger. On the left side of the trachea, about the level of the arch and slightly compressing it, was a large tumor mass, 3 cm. in length, and 2 cm. in diameter. This mass was without pigmentation. Esophagus. typical squamous celled carcinoma, occupies the middle and lower thirds of the esophagus about 10 cm. in length, extending through all the coats of the esophagus and almost obliterating the lumen, with metastases in the para-

vertebral glands. The remaining parts of the body were remarkably free from metastases, a few melano-sarcomata being found in the left kidney and suprarenal. The nevus was examined but did not show any carcinomatous proliferation.

Cases 2 and 3 are both from the University of California Service.

Case 2. Was a woman, aged 44, who for a number of years had intestinal trouble of a character which was diagnosed as tubercular, as she had an old tubercle of the lung. There was persistent occult blood in the stools, pain, marked constipation, neither loss nor gain in weight. At operation, the ileum was resected for a tumor, which had caused considerable stricture and the appendix was removed for another tumor. There were multiple adhesions which were separated. The patient remains well today. On microscopical section the tumor of the ileum proved to be a carcinoma and the appendix an adeno-carcinoma.

Case 3. The third case was a girl, 22 years of age, who entered the hospital complaining of pain in the left leg and lumbar region. Abdomen: no tumor felt. Visible peristalsis in the epigastrium. Vaginal examination revealed a tumor of the left ovary. Spine stiff, almost immovable, muscle spasm marked, greater on the right.

At autopsy: A carcinoma of the stomach and gastric lymph nodes with metastases to the vertebrae and a mixed tumor of the ovary.

These cases are by no means as rare as has been supposed. Harbitz² in the Journal A. M. A., for March 25, 1916, has given his findings in 3613 autopsies extending over a period of 15 years. He found cancer in 14.5 per cent. of all cadavers. In 103 cases multiple tumors were found, i. e. in 2.8 per cent. This includes, however fifty-one cases of associated malignant and benign tumors, and sixteen cases of multiple cancers of different types. This latter group forms 0.44 per cent. of the cancer cases. In two cases both sarcoma and carcinoma were found separately and in two cases combined. In one case there were three separate carcinomas, and in two others carcinoma was associated with glioma or endothelioma.

In animals, on the contrary, multiple growths are quite frequently encountered, both as spontaneous and inoculable tumors, which, experimentally, have been found to throw considerable light on the problems of cancer. Many writers are of the opinion that such cases of multiple growths are purely accidental and are of no value in the study of the general problems of carcinoma. Others, as Adami,³ consider them to be of great value in the elucidation of the nature and etiology of malignant growths. Adami considers them to indicate not merely a lowering of tissue resistance, but of general body resistance; so that, simultaneously, cells in various parts find conditions possible for active and independent proliferation. It is, however, not of so much importance what is the type of growth, as what is the system or tissue from which the growth originates. Behind the "immediate" stimulus to proliferation, or the exciting factor, whether it be parasite or infection, a misplaced embryonal rest, or senile involution, there is a disturbance in the biological character of the cell which determines whether it is to be cancerous or not. This modification in the properties of the cell or tissue is to be regarded as the primary factor. Hauser refers to this theory as "carcinomatous disposition," and Ribert mentions

the idea of a general biological change as the cause of new growths. Among the benign growths, we meet with many examples of multiple tumors. Here it is one form of tissue only that is affected and this would again seem to indicate that the tissue is especially susceptible to the formation of aberrant growths.

There is such a thing as a general neoplastic tissue disposition, and tumors are the result. While it is rare for both the *stroma* and the *epithelial* structure to become malignant at the same time, yet cases are fairly common where both structures have undergone a simultaneous malignant degeneration. In 1901, Wells⁴ reported three cases of so-called sarco-carcinomas developing in the thyroid gland. This tumor was a *carcinoma* whose *epithelial* elements were meshed in a sarcomatous stroma, and the metastases were both clearly sarcomata or carcinomata. Herxheimer, in 1908, collected twenty cases and included one from the esophagus.

Woglon reports an interesting case of a carcino-sarcoma in a mouse, in which there were two spontaneous tumors, one in the left axilla and one in the right groin. The tumor in the groin was found to be a carcino-sarcoma, while that in the axilla proved to be a pure sarcoma. Woglon believes that this sarcoma was primarily a carcinoma, and that the sarcoma had overgrown the carcinoma. It is well known that in transplantable carcinoma, possessing the power to initiate sarcoma development in their stroma, the sarcomatous portion gradually gains the ascendancy over the carcinomatous, and there is no reason to suppose that this rule would not be valid in the case of spontaneous new growths.

Ehrlich has explained the onset of sarcomatous transformation in the carcinoma, by assuming that the animal in which it takes place, has some special predisposition toward connective tissue proliferation, as some human beings, for example, are apt to develop keloids at the site of a scar. Ehrlich and Apolant inoculated a typical adeno-carcinoma through ten generations and finally obtained a mixed tumor, the stroma of which was a spindle-celled sarcoma. In the thirteenth generation, the carcinoma had disappeared and was replaced by a sarcoma which persisted as a sarcoma as late as the twenty-sixth generation. Harbitz cites three new cases in the human of a sarcoma developing secondarily on an abdominal metastatic carcinoma from an ovarian cancer. In some cases where the primary tumors are close together, though entirely separated, several authors, as Adam and Wooley, have assumed a local predisposition or susceptibility.

Many of the reported cases of multiple tumors are bilateral, occurring in the ovaries and the testicles, the kidneys and adrenals. Zangmeister found that out of thirty-nine sarcomas of the ovaries, ten were primarily bilateral. Pices, in a series of twenty-three cases of sarcoma of the ovaries, found nine bilateral primary sarcomas. Kober, in a study of 114 cases of malignant testicular tumors, found five bilateral instances. Rolleston and Marks found two primary bilateral cases of malignant diseases of the adrenal in a study of twenty-six cases. Huster found thirteen primary bilateral cases of malignant tumors of the kidney

in a series of 607. These cases would tend to show that there is a probable predisposition of the tissue involved, and that the tumor formation occurs with an adequate stimulus. This predisposition is most likely a development disturbance.

Whether such tumors as the melano-sarcoma and esophageal carcinoma are related or arise from a single focus, it would be impossible to state. However, the experimental work on animal neoplasms has shown several analogies, and such an origin is not entirely improbable. Different types of tumors frequently occur in a single animal. Of the forty-nine animals used in the experiments of Tyzzer, eleven presented tumors of two types, and one, primary tumors of four types. In the latter there was hypernephroma, a lymphosarcoma, a papillary cystadenoma of the lung and an adeno-carcinoma of the lung. About 25 per cent. of these cases, therefore, presented multiple tumors of different types. Multiple primary tumors were probably present in a far greater proportion, for in many cases the lung tumors were multiple and occurred, not only in single, but in several lobes. Many of the tumors which develop spontaneously in mice and rats can be inoculated in animals of a similar species. That this is a real transplantation of tumor cells, and not an irritative lesion of the tissue of the host, can be shown by careful microscopical examination of the tissue. The stroma of the inoculated tissue undergoes necrosis and a new stroma is furnished from the connective tissue of the host.

Hanaio, in 1899, was the first to show that these tumors could be inoculated. In the succeeding decade numerous investigators produced various inoculations and were able to carry them through many generations. These tumors may show considerable changes in cellular type during successive generations. Loeb and Ehrlich demonstrated that a carcinoma could be changed into a sarcoma, and Flexner and Jobling have also given proof that a sarcoma can be transformed into a carcinoma. Apolant, in his experiments in partially immunized animals, has shown that carcinoma may become adenomatous in structure. Such changes as these are of importance in the virulence of the tumor. Miss Slye⁷ states that it is her experience that when a cancer is put into a strain where it has not occurred before, it tends to appear in the form of a sarcoma. It appears that the more embryonal tissue yields first to the formless proliferation of cancer. As cancer becomes more deeply seated in a strain, the more highly differentiated tissues yield and carcinoma becomes the dominant form of neoplastic growth. All the strains long cancerous show tremendous predominance of carcinoma over sarcoma. This seems to be correlated with the fact that as the cancer ancestry behind a strain deepens, more and more of the tissues show the tendency to neoplastic growth; so that multiple tumors are more common than single growths in a family in which cancer is old.

The development of sarcoma in animals inoculated with epithelial tumors is regarded by most investigators as the result of the irritating influence of the tumor epithelium.

Infection versus Tumors.

Adami has called attention to a certain parallelism which exists between the behavior of infections and that of tumors. In infections there is usually a single focus, and when multiple foci exist these most commonly occur simultaneously. From this he concludes that the products of the original focus have aroused the protective agency of the body to produce antibodies and thus limit the spread of the infection. It may be also in cancer that the products of the new growth produce a reaction in the tissue of the host, which, though not sufficient to inhibit the original growth, are yet sufficient to prevent a further extension in the body. Gaylord has shown that in a certain number of mice, where the inoculation of tumors has been successful, these tumors will subsequently disappear. If now it be attempted to reinoculate them with the same or similar forms of growth, the result is negative. Sticker also observed that he could inoculate a tumor successfully in one area of the mouse, but could not reinoculate it in another portion of the anatomy at the same time; also, that if the inoculations were made in two different places at the same time, both would take, but if it were attempted to inoculate them at different periods of time the result would be negative.

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BORDERLINE TYPES OF SEBORRHOEIC DERMATITIS AND PSORIASIS.*

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The study of borderline types is of very great importance to Dermatology for the specific reason that dermatological classification is still resting on shifting, unstable and manifold bases. None of the fundamental factors taken as a basis of various systems of dermatological classifications can consistently and definitely divide the recorded nosological material into distinct and sharply defined groups without overlapping, conflicting and leaving a surplus of nondescript and undefined clinical forms.

Pathology, etiology, morphology, anatomic structure and clinical symptomology—all of these factors have been found insufficient to be taken individually as a sole guiding principle of classification. The most shifting and variable among these factors is morphology, on which essentially the entire clinical symptomology and differentiation of the bulk of individual dermatoses is built, even though, as groups, they are divided on pathological differences. For this reason the study of borderline dermatoses assumes more than a casuistical interest; it is

more than a mere refinement of differential diagnosis. The study of borderline dermatoses can and should be utilized for a broader and more important purpose of bringing out new viewpoints and facts of their clinical and pathological relationship, thus preparing new bases for a rational and comprehensive classification.

Among various borderline dermatological types those between psoriasis and seborrhoeic dermatitis are of considerable practical and theoretical interest.

It has been the writer's privilege to see for the last two years several of these cases. The borderline features of the cases were so marked as to make a differential diagnosis well nigh impossible and to prompt their record.

CASE REPORTS.

Case 1. Mrs. B., æ. 36, came with a generalized eruption of several years' duration. The scalp was covered with a fairly dry but heavy diffuse crusting extending way below the hairline. Large typical patches of seborrhoeic dermatitis between the breasts. On the back and limbs a number of patches from a dime to a dollar sized, of frankly psoriatic type; there are also patches with heavy yellow scales suggestive of seborrhoeic dermatitis. Knees and elbows are free from eruption. The patient gives a history of a chronic course with many relapses.

Case 2. A young girl æ. 16, came with dry, scaly typical psoriatic patches on both elbows; there were also dry, crusting large areas on the scalp. The case was diagnosed as psoriasis. Great was our surprise when a week later the patient came with as a typical acute outbreak of seborrhoeic dermatitis, as one may meet. A number of round and circinate patches on the face and neck were clearly the outgrowth of the main seborrhoeic area on the scalp spreading downward over the hairline in all directions. Psoriatic patches on the elbows looked as before. Several patches on the back presented the combined features of both conditions.

Case 3. Mrs. M., æ. 25, shortly after confinement came with an acute breaking out of the whole scalp, face and neck. The examination reveals a classical picture of a hyperacute seborrhoeic dermatitis. The trunk of the body and the limbs show several scattered patches presenting a mixed picture of psoriasis and seborrhoeic dermatitis. The knees and the elbows on the extensor surface show dry patches which are nearer to the pure type of psoriasis than any other patches. The patient states that these patches are of many years' duration with many recurrences. The patient's two brothers are affected with psoriasis.

Case 4. Mr. S., æ. 45, paralyzed and bedridden for the last 13 years. The advice was sought for, what was deemed, bed sores which developed gradually during the last few months. The examination has revealed several large, from a dollar to a hand palm sized, psoriatic patches on both buttocks and extending further down in the genito-crural region, where it was associated with an erythema intertrigo due to the soiling by urine and feces. Some dry scaling on a reddened base was also present on the scalp and bearded region of the face. Elbows and knees showed small psoriatic patches. The patches on the buttocks showed a decidedly yellow tinge and rather heavy plate-like

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